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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,886	04/11/2005	Tamaki Oda	Q87392	4706
23373	7590	03/13/2006	EXAMINER	
SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			NOAKES, SUZANNE MARIE	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/530,886	Applicant(s) ODA ET AL.	
	Examiner Suzanne M. Noakes, Ph.D.	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 4-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 June 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>30 June 2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-3 in the reply filed on 17 February 2006 is acknowledged.

Status of Claims

2. Claims 1-10 are pending. Claims 1-3 are under examination and claims 4-10 are withdrawn from further consideration for being drawn to non-elected inventions.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 30 June 2005 has been considered by the examiner. See signed and attached PTO-1449.

Claim Objections

5. Claims 1-3 are objected to because of the following informalities: in the first instance of the acronym CAP, the words for which they stand should be spelled out followed by CAP in parenthesis (see line 7, p. 1 of the specification for a proper example). Appropriate correction is required.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The polypeptides as claimed, have an amino acid sequence duplicative of that of the protein designated as SEQ ID No: 2 and 4 or the cellular precursor thereof and possesses the biological and functional properties of the naturally occurring polypeptide that binds c-Cbl-associated proteins and therefore does not constitute patentable subject matter absent recitation of "isolated and purified" in the preamble.

See *American Wood v. Fiber Disintegrating Co.*, 90 U. S. 566 (1974); *American Fruit Growers v. Brogdex Co.*, 283 U. S. 1 (1931); *Funk Brothers Seed Co. v. Kalo Inoculant*, 33 U. S. 127 (1948); and *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 112 – 2nd Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "homology" as used in context with a percentage is incorrect. Homology has an accepted use in referencing protein or DNA sequences in

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one of two ways: a) in the context that they share a common ancestor or b) that two sequences share a common function. Thus, there is no degree of homology; it exists or it does not. Therefore trying to claim proteins that are "90% homologous" is indefinite. The examiner suggests the phrase "identity" more appropriately describes what Applicant's are actually attempting to claim.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement:

10. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for CAP binding proteins according to SEQ ID No: 2 and 4, does not reasonably provide enablement for variants comprising these sequences with 1-10 substitutions, deletions or additions thereof, or alternatively those that have 90% sequence identity thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims without undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some

experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are directed to the CAP binding proteins comprising the amino acid sequence set forth in SEQ ID No: 2 or 4 or biologically active variants thereof having an amino acid sequence at least 90% identical to the amino acid sequence given in SEQ ID No: 2 or 4 (claim 2), or those that comprise SEQ ID No: 2 or 4 which may have 1-10 amino acids added, substituted or deleted therefrom. The specification discloses isolated CAP binding protein consisting of the amino acid sequence set forth in SEQ ID No: 2 or 4. The specification further establishes that this protein specifically binds to CAP which is involved in the insulin signaling transduction pathway, and provides as assay for this binding activity. General guidance is given regarding how to make and test variants of any protein. The scope of patent protection sought by Applicant as

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defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons. The problem of prediction protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable of success is limited. Certain positions in the sequence are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions at all (see Bowie et al. pp. 1306-10, specifically p. 1306 column 2, paragraph 2; Wells pp. 8509-8517). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. by amino acid substitutions or deletions or insertions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active protein variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the

ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon the surrounding residues; therefore substitution or non-essential residues can often destroy activity. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and screen the same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which established the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Written Description:

11. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that written description for a genus can be achieved by describing a representative number of species within a broad genus. Claims 1 and 2 are broadly generic to a multitude of possible variants of a polypeptide comprising SEQ ID No: 2 or 4 which can have 1-10 substitutions, deletions or additions (claim 1) or which

are 90% similar to SEQ ID No: 2 or 4 (claim 2), but which still retains the capacity to bind c-Cbl-associated protein (CAP). Thus, the possible variations are enormous to any class of potential CAP polypeptides of SEQ ID No: 2 or 4 with different structure or varying degrees of functionality. Since the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of CAP bind proteins beyond those disclosed in the examples in the specification. Moreover, the specification lacks a sufficient variety of species to reflect this variance in the genus since the specification does not provide a sufficient number of examples of variants which comprising SEQ ID No: 2 or 4 which bind to the CAP proteins.

While having written description of the polypeptide comprising SEQ ID No: 2 and 4 identified in the specification and examples, the specification is limited to a select few polypeptides that may qualify under the broad genus but this is in no way indicative or representative of the broad genus because the number of possibilities extend into the thousands.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984)

(affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

13. Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Strausberg et al. (PNAS, Dec. 2002, 99:16899-16903). Strausberg et al. teach a 275 amino acid protein that is 96.6% identical to SEQ ID No: 4 (the first 172 amino acids are identical) and 94.9% identical to SEQ ID No: 2 (see attached sequence alignments).

Thus, inherently the proteins will be able to bind CAP.

14. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Cronshaw et al. (J. Cell Biology, Sept. 2002, 158(5):915-927). Cronshaw et al. teach a polypeptide that is overall 96% identical to SEQ ID No: 2 (100% identical from amino

acids 2-169). The polypeptide is 271 amino acids in length but with such high sequence identity will inherently bind CAP.

15. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Noakes, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached on Monday to Friday, 7.30am to 4.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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02 March 2006

Handwritten signature: H. H. Hoachy

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